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TRADITIONAL HERBAL FOLK MEDICINE USED FOR CONTROLLING CORONA VIRUS (SARS-COV-2) DISEASE (COVID-19)

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ABSTRACT

This review paper developed on the basis of literature survey highlights the use of traditional herbal folk medicine for controlling the deadly outbreak of corona virus (SARS-CoV-2) mutants, Delta variant (B.1.617.2) and Delta Plus (AY. 1) causing major health issue with the highest viral infections and deaths. Severe acute respiratory syndrome (SARS-CoV-2) is a pandemic respiratory infections viral disease. SARS-CoV-2 syndrome is also causing an unusual type of pneumonia leading to the lungs infection. Botanical drugs constantly become a worthy therapeutic alternatives against viral infections including corona virus (SARS-CoV-2). Therefore, there is an urgent need for the agents that can act against SARS-CoV-2 as a precautionary measures which boost our immunity during Covid-19. In this review paper, there are many medicinal plants listed have been found inhibited the SARS-CoV-2 viral replications, and acts as immunity booster. The use of spices and herbs may also play a significant role against viral infections. Therefore, herbal and dietary therapy plays significant role in controlling many infectious diseases including corona virus (SARS-CoV-2) affecting human health. However, there is no clinical evidence to support herbal medicine as remedy for corona virus and warranted further scientific evidence. Further detailed clinical trial experiments should be conducted for the scientific validation. This review paper updates about plants either used as expression patterns for plant based vaccines or as antiviral drugs as a medicine for controlling SARS-CoV-2 outbreak since the disease is becoming endemic.

Keywords: Antiviral, corona, covid-19, herbal medicine, immunization, mutants, vaccine.

INTRODUCTION

The outbreak of second wave of corona virus (SARS-CoV-2) mutants, Delta strain (Delta (B.1.617.2) and Delta Plus (AY.1) throughout the world has created major health problems (1-10). The infection rate is very high as compared to original Wuhan novel corona virus. The Delta variant (B.1.617.2) is a result of the double mutation in the corona virus (SARS-CoV-2). One mutation increases the transmissibility of this variant and the second mutation increases its probability of escaping or avoiding the efficacy of the vaccine (1-10). According to WHO report, everybody is vulnerable and people should continue to using masks and to avoid crowds, even if they're fully vaccinated.

Indonesia has become the new epicenter of the pandemic, surpassing India and Brazil to become the country with the world's highest count of new viral infections (1-10). In Indonesia, viral infection cases and deaths have skyrocketed as the highly contagious delta variant is spreading very quickly in the densely populated areas leading to the more hospitalization and deaths. At present situation, hospitals are overcrowded, and people are struggling to get bed facilities, insufficient oxygen supply, and poor medical supplies. Therefore, infected people stay away from the hospitals, resulting in more number of deaths at home. The surge is part of a second wave across Southeast Asia, where vaccination rates are low but countries had, until recently, contained the virus relatively well. Vietnam, Malaysia, Myanmar, India, USA, UK, Brazil, Spain, Italy, Portugal and Thailand are also facing their largest outbreaks yet and have imposed new restrictions, including lockdowns and stay-at-home orders. Delta is wreaking havoc in Spain, Portugal and the United Kingdom. Spain alone reported nearly 44,000 cases, doubling the number recorded one week ago. Delta variant in Europe is largely affecting unvaccinated 15- to 30-year-olds, experiencing it as a bad cold, the upsurge in new cases presents a hazard for all and are getting long-haul COVID and potentially neurologic disability. Hospital admissions are quickly rising in Europe, and the spread of the virus has the potential to infect those already vaccinated (1-10).

Severe acute respiratory syndrome corona virus (SARS-CoV-2) is a novel corona virus known for the global pandemic (11-20). The corona virus (SARS-CoV-2) outbreak is significantly increasing throughout the world and the disease continues to spread at an alarming rate despite to constrain the pandemic (11-25). Epidemiological investigations have suggested that the outbreak was associated with a seafood market in Wuhan (11-60). The corona virus disease is highly transmittable leading to more infections. Severe acute respiratory syndrome (SARS-CoV-2), an emerging respiratory infectious disease presented a major threat to public health (11-30). Corona viruses belong to the family *Coronaviridae* in the order *Nidovirales* have the largest genomes (30 Kb) of all RNA viruses (12-55). Corona viruses are actually a family of hundreds of viruses, and corona represents crown-like spikes on the outer surface of the virus therefore, named as a corona virus (13-60). The corona virus (SARS-CoV-2), is zoonotic infecting both animals and human and WHO declared corona virus disease (COVID-19) as a global pandemic (1-60). Therefore, SARS-CoV-2 infecting animals to human population is one of the best example of zoonotic origin (13-70). Furthermore the sequence analysis confirmed that SARS-CoV-2 has been originated from bats (4-59).

The corona virus (SARS-CoV-2) designated as COVID-19 prominently affect the respiratory tract (both lower and upper

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respiratory tract), with the initial symptoms of common cold, fever, dry cough, throat infections, fatigue, general feeling of being unwell, runny nose, aches and pains, nasal congestion, loss of taste or smell, loss of speech or movement, headache, sore throat, a rash on skin, or discoloration of fingers or toes, conjunctivitis, shortness of breath, chest pain or pressure, and diarrhea to severe pneumonia, difficulty in breathing and ends with the patient death (5-55). Infection with these highly pathogenic corona viruses (SARS-CoV-2) could result in the acute respiratory distress syndrome (ARDS) and acute lung injury (ALI) followed by the failure of the lung function and death (6-57). The incubation period of the corona virus (SARS-CoV-2) disease is 14 days and the time from the onset of symptom to developing pneumonia is 4 days (1-46). Therefore, corona virus (SARS-CoV-2) has become a major threat to the human population (1-47).

Airborne transmission, particularly *via* nascent aerosols from human atomization, is highly virulent and represents the dominant route for the transmission of COVID-19 disease (14-59). Inhaled virus-bearing aerosols deposit directly along the human respiratory tract (15-48). The global pandemic corona virus (SARS-CoV-2) was circulating in bat populations and its cross-species transmission events leading to outbreaks in humans (17-55). Human infecting corona viruses have been classified into seven different categories (1-40). The first corona virus was discovered in chickens in the 1930s. Human corona viruses were first identified in the mid-1960s (1-54). The first corona viruses discovered in mid-sixties were able to infect humans are 229E and OC43 (1-49). At the end of December 2019, the outbreak of corona virus caused by severe acute respiratory syndrome corona virus (SARS-CoV-2) occurred in Wuhan, Hubei, China (1-48). The novel virus was named as Wuhan corona virus or 2019 novel corona virus (2019-nCov) by the Chinese researchers (30-55). The International Committee on Taxonomy of Viruses (ICTV) named the virus as SARS-CoV-2 and the viral disease as COVID-19 (1-53).

RNA viruses are characterized by a high mutation rate, up to a million times higher than that of their hosts (20-59). Mutation is very high in RNA-based viruses like SARS-CoV-2 (1-50). Viruses mutate because they're constantly making copies of themselves in enormous numbers (20-52). Within a human body, a virus can replicate itself millions or billions of times (20-50). Furthermore, the genome sequence of corona virus (SARS-CoV-2) also showed phylogenetic similarity to one of the species of bats (80%) (1-50). Therefore, corona virus (SARS-CoV-2) is originated from bats and bats are the primary hosts for the spread of the COVID-19 disease (1-50). The large SARS-CoV-2 genome is a polyadenylated RNA of 29,727 nucleotides, which is capped, infectious and encodes four major viral structural components, the spike glycoprotein (S), envelope (E), membrane (M), and nucleocapsid (N) proteins, and the 16 non-structural proteins (1-48). The spike glycoprotein (S) is an attractive target for the vaccine production because it facilitates the viral entry into the host cell during the virus infection process (2-55). The spike glycoprotein (S) protein of the corona virus is the major target for neutralizing antibodies (1-30, 47).

Synthetic drugs such as Ivermectin is a potent inhibitor of SARS-CoV-2 infections with excellent ability to suppress the pathogenic virus against *in vero*-h SLAM cells model) (1-47). However, remdesivir, chloroquine, hydroxychloroquine, favipiravir/favilavir have not given satisfactory results when used as antiviral agents against SARS-Co-2 (1-40, 57). A vaccine for the virus that causes COVID-19 would be an ideal approach to achieving herd immunity (1-54). Several corona viruses, such as severe acute respiratory syndrome-related corona virus (SARS-CoV-2) and Middle East respiratory syndrome-related corona virus (MERS-CoV) are the virus pandemics (1-53).

Nanotechnology benefits from the modern vaccine design since nonmaterial's are ideal for antigen delivery, as adjutants, and mimics the structural features of viruses (3-51). Nanotechnology has paved new pathways and provided a new avenue in the vaccine development for the infectious diseases, such as COVID-19 (4-55). Nanotechnology has a potentiality in COVID-19 treatment and vaccine development. Nanoparticles triggered the antigen-specific immune responses and helped in the smooth delivery of the antigen into the host cell (1-53). Nanoparticle-based antigen delivery has many advantages than traditional vaccine delivery system such as safe delivery vehicles, vaccine adjuvant, improved antigen stability, targeted delivery, long-time controlled release and evasion of immune responses (1-50). Hence nanotechnology approaches in vaccine development and immunoengineering become very powerful platforms (1-59). Moderna Inc., biotechnology company in collaboration with Vaccine Research Center at the U.S. National Institutes of Health, has developed mRNA vaccines (mRNA-1273) encapsulated in lipid-based nanoparticles (1-59). Furthermore, mRNA vaccine (BNT162b2) developed by Pfizer-BioNTech can be considered as a great achievement of nanomedicine (20-57). An mRNA-based vaccine employing lipid nanoparticles (LNPs) delivery is successful (20-60).

Corona virus (SARS-CoV-2): Botanical drugs

Plants are one of the most important sources of medicines (62-179). The use of traditional folk medicinal herbs has become an important part of daily life despite the progress in modern medical and pharmaceuticals research (63-119). The tribal and rural people of India depends on the crude preparations of these medicinal herbs for a number of treatments (66-166). Medicinal plants are useful for curing human diseases and play an important role in healing due to the presence of photochemical constituents (55-189). The use of the herbal remedy is not only cost effective but also safe and almost free from serious side effects (60-179). The rural communities rely greatly on indigenous herbal medicines for the health care since herbal medicines are readily available, safe and cost effective (57-190). Use of medicinal plants are time-tested and used by people worldwide and no side effects and cost effective compare to other system of medicine (67-150).

India is called the pharmacy of the world during the COVID-19 pandemic with its vast experience and deep knowledge in herbal medicine. India is one of the world's biggest drug-makers and an increasing number of countries have already approached India for procuring corona virus vaccines. Indian traditional herbal system of medicine known as *Ayuverda* also played an important role during corona virus (SARS-CoV-2) outbreak. Traditional medicines involving plant-based formulations have proven successful in boosting immunity and providing tolerance to the virus infections (70-190). Herbal medicines of antiviral activity are of great interest and have been widely explored (60-190). Plant derived medicines have played a pivotal role in the health care (59-190). Many of these natural products have pharmacological or biological activity that can be exploited in pharmaceutical drug discovery and drug design (61-178). Herbal medicines of antiviral activity are of great interest and have been widely explored (63-190). Plant based antiviral compounds can block or inhibit virus replication cycle by interfering with virus attachment to cells, interfering with viral enzymes or suspending viral genome replication (60-179). Plant production platforms are being used to generate vaccines and antiviral proteins inexpensively at mass scale. Furthermore, the extraction and identification of new antiviral compounds have significant role in the development of therapeutic botanical drugs (65-175). Phytodrugs also played an important role as antiviral compounds and inhibited SARS-Cov-2 activity (55-180). Plant-based vaccines are safe, economical,

exhibited immunogenicity, and protection against different viral infectious diseases (60-188). There are many medicinal plants which have been used for controlling corona virus (SARS-CoV-2) outbreak and have been documented and listed in the following tables-1, 2 and 3 (65-198). These plants were basically used as immunity booster, some of them have been found inhibiting the SARS-CoV-2 replication under *in vitro* and animal model studies (62-198). Therefore, there is a ray of hope for the development of herbal antiviral drugs against corona virus (SARS-CoV-2) (63-196). Plants were also used as the expression platforms for the production of antigenic protein. This plant based antigenicproduction could be used for the mass immunization programs to combat the corona virus (SARS-CoV-2) (60-198). In addition to this, consumption of the m edicinal plants as a part of herbal and dietary therapy could also help in controlling this deadly corona virus (SARS-CoV-2) disease (covid-19) (61-199).

Table-1: Medicinal plants used for controlling the infections of SARS-CoV-2

No	Plant name	Family	Parts used	Therapeutic uses during outbreak of SARS-CoV-2
1	Curcuma longa (Turmeric: Arishina in Kannada)	Zingiberaceae	Rhizome & root	Antioxidant , antiinflammatory properties, Antiviral, remedy for high fever, cold, cough, throat infections. (Key ingredient in Indian masala tea)
2	Zingiber officinale (Ginger) (Aadrak or Shunti)	Zingiberaceae	Root or rhizome	Antioxidant, Remedy for sore throat, cold, and cough and acts as a immunity booster. (Key ingredient in Indian masala tea)
3	Glycyrrhiza glabra (Mulethi or Liquorice) (Yashtimadhu)	Fabaceae	Root	Antiviral, remedy for sore throat, cold, cough, and acts as a immunity booster. Inhibited SARS-CoV-2 activity under in vitro and animal studies. Consumed in Indian tea
4	Artemisia annua	Asteraceae	Aerial parts	Antioxidant, Antimalarial and antiviral activity. SARS-CoV-2 inhibitor under in vitro and animal studies.
5	Azidarachta indica (Neem)	Meliaceae	Aerial parts	Antiviral, antibacterial, antifungal remedy for sore throat, cold, cough, and acts as a immunity booster
6	Ocimum sanctum (Tulsi)	Lamiaceae	Whole plant	Antioxidant, Antiviral, remedy for sore throat, cold, cough, and acts as a immunity booster (Key ingredient in Indian masala tea)
7	Tinospora cordifolia (Guduchi or Giloy) (Amruthballi in Kannada)	Menispermaceae	Whole plant	Antioxidant, Anti-inflammatory, antiviral properties helps in tackling respiratory problems like cough, cold, and breathing. SARS-CoV-2 inhibitor under in vitro and animal studies
8	Picrorhiza kurroa (Kutki)	Scrophulariaceae	Root or rhizome	Immunity booster, antiviral activity
9	Triphala (A mixture of 3 plants) Emblica officinalis Terminalia bellerica Terminalia chebula	Euphorbiaceae Combretaceae Combretaceae	Aerial parts	Antioxidant Rejuvenation, antiviral activity, throat infections, immunity booster SARS-CoV-2 inhibitor under in vitro and animal studies
	Phyllanthus emblica (Indian gooseberry) +	Euphorbiaceae Liliaceae	Aerial parts	Antioxidant Decoction is Immunity booster, throat infections. Potent rejuvenator and immunomodulator
10	Aloe vera (Aloe barbadensis) juice			SARS-CoV-2 inhibitor under in vitro and animal studies Antioxidant, Remedy for the throat infections
11	Syzygium aromaticum (Clove; Lavang)	Myrtaceae	Flower buds	Antiinflamatory, antiviral properties Immunity booster (Key ingredient in Indian masala tea)
12	Toona sinensis (Chinese toon)	Meliaceae	Leaves	Antimicrobial, antiviral properties
13	Cinnamomum verum (Cinnamon; Dalchini)	Lauraceae	Stem bark	Remedy for throat infections since bark has antiviral properties (Key ingredient in Indian masala tea)
14	Adhatoda vasica	Acanthaceae	Whole plant	Asthma, bronchitis, cough, diarrhea, dysentery, fever, flu. Antiviral properties
15	Andrographis paniculata (Green chiretta)	Acanthaceae	Whole plant	Antiviral properties, immunity booster. Remedy for controlling fever, throat infections,
16	Swertia chirata	Gentianaceae	Whole plant	Antiviral, throat infections and immunity booster

Table-2: **Medicinal plants used for controlling the infections of SARS-CoV-2**

No	Plant name	Family	Parts used	Therapeutic use during outbreak of SARS-CoV-2
16	Moringa oleifera (Drumstick; Nuggekai)	Moringaceae	Aerial parts	Antioxidant, Antiviral, and remedy for high fever, cold, cough, throat infections Immunity booster
17	Torreya nucifera	Taxaceae	Seed, leaf	Antiviral, Protease inhibitor
18	Hibiscus sabdariffa (Rosella)	Malvaceae	Aerial parts	Antiviral, antifungal and antibacterial activity
19	Cichorium intybus (chicory)	Asteraceae	Whole plant	Antiviral properties and antimicrobial
20	Chrysanthemum coronarium	Asteraceae or Compositae	Aerial parts	Antiviral, remedy for sore throat, cold, cough, and acts as a immunity booster Consumed as vegetable
21	Nigella sativa (Black cumin seeds)	Ranunculacea	Aerial parts	Antiviral, immunity booster
22	Anastatica hierochuntica	Cruciferae	Aerial parts	Antiviral properties
23	Psidium guajava (Guava)	Myrtaceae	Aerial parts Leaf, fruits	Antiviral, and acts as a immunity booster
24	Houttuynia cordata (chameleon plant)	Saururaceae	Whole plant	Antiviral, and acts as a immunity booster Consumed as vegetable
25	Myrica rubra Scutettaria baicalensis Asplenium belangeri	Myricaceae Lamiaceae Aspleniaceae	Aerial parts	Antiviral activity
26	Galanthus nivalis (Snowdrop)	Amaryllidaceae	Aerial parts	Lectins are potential inhibitors, antiviral Immunity booster
27	Lycoris radiata	Amaryllidaceae	Aerial parts	Lycorine, an alkaloid has potential inhibitors, antiviral
28	Cinchona officinalis (Quinine plant)	Rubiaceae	Bark	Bark has the antiviral properties
29	Euphorbia neriifolia (Indian Spurge Tree)	Euphorbiaceae	Aerial parts	Antiviral properties and antiinflamatory
30	Cymbopogon citratus (Lemon grass)	Poaceae	Leaf	Antiviral and key ingredient in tea. Remedy for cold, throat infections

Table-3: **Medicinal plants used for controlling the infections of SARS-CoV-2**

No	Plant name	Family	Parts used	Therapeutic use during outbreak of SARS-CoV-2
31	Rauvolfia serpentina (Indian snake root)	Apocynaceae	root	Antiviral (Aescin isolated)
32	Aesculus hippocastanum (Horse chestnut)	Sapindaceae	Aerial parts	Antiviral and (Reserpine isolated)
33	Withania somnifera (Ashwagandha)	Solanaceae	Leaves, root	Withanone significantly down regulated TMPRSS2 in MCF-7 cells. Withanone
34	Alpinia officinarum (Lesser galangal)	Zingiberaceae	rhizome	Antiviral properties Remedy for sore throat, cold, cough, and acts as a immunity booster
35	Boesenbergia rotunda (Finger root)	Zingiberaceae	rhizome	Antiviral, remedy for sore throat, cold, cough, and acts as a immunity booster. Panduratin A isolated
36	Thapsia garganica (Deadly carrots)	Apiaceae	Fruits, root	Thapsigargin has antiviral activity SARS-CoV-2 inhibitor under in vitro and animal studies
37	Saposhnikoviae divaricate (Fang Feng or Bangpung)	Umbelliferae	root	Immunomodulator, antiviral, and acts as a immunity booster.
38	Polygonum multiflorum (Buckwheat)	Polygonaceae	Root, leaf	Antiviral, remedy for throat infections, cough, and acts as a immunity booster Antiviral activity.
39	Agastache rugosa (Korean Mint)	Lamiaceae	Aerial parts, oil	Remedy for sore throat, common cold, cough, and acts as a immunity booster (Key ingredient in Korean tea)
40	Pyrrosia lingua (Tongue fern)	Polypodiaceae	Aerial parts	Antiviral and used as a general medicine. Antiviral, immunity booster and used as general medicine
41	Brassica juncea (Indian mustard)	Brassicaceae	Seeds, oil leaves	Effective modulation of ACE2 and TMPRSS2 receptors
42	Cissampelos pariera (Velvetleaf; Padavali)	Menispermaceae	Aerial parts	Leaf and fruit juice has antiviral activity
43	Camellia sinensis (Green tea)	Theaceae	Leaves	Antiviral activity, immunity booster, therapeutic value
44	Andrographis paniculata (Green chiretta)	Acanthaceae	Aerial parts	Antiviral, Immunomodulator, anti-HIV
45	Momordica charantia (Bitter melon;Hagalakai)	Cucurbitaceae	Fruits, leaf	Antiviral, antifungal and immunity booster

CONCLUSION

In this review paper, the use of medicinal plants combating SARS-CoV-2 has been highlighted and listed. Among the listed medicinal plants, some of the medicinal plants showed antiviral activity, others under *in vitro* conditions, and animal studies demonstrated the blockage or inhibited the SARS-CoV-2 activity. Furthermore, foods and herbs possess a potential antiviral ability against SARS-CoV-2 and can prevent COVID-19. This has opened a new ray of hope for developing traditional herbal medicine remedies for SARS-CoV-2 infection. However, subsequent *in vitro* and *in vivo* experiments are needed to elucidate their efficacy against SARS-CoV-2 is lacking and not sufficient. Future epidemiological and clinical studies are required to further assess the benefits of herbal medicines for the prevention of SARS-CoV-2. Although some herbal medicines have promising potential and are widely used, many of them remain untested and their use also not monitored. Regulatory framework should also be applied immediately to ensure that botanical drugs to conform with required standards of safety, quality, and efficacy. However, these hypotheses require experimental validation in SARS-Cov-2 infection models and COVID-19 patients. In addition, subsequent *in vitro* and *in vivo* experiments are needed to elucidate their efficacy against SARS-CoV-2. Therefore, data presented in this review paper is not sufficient and herbal interventions remains weak and lacking. Furthermore, there are many experimental issues and data presented is not enough for the scientific validation. Finally, there is a possibility that these treatments might be associated with the induction of harmful effects. In addition, preclinical and clinical trial evaluations of these herbal agents for COVID-19 have not specifically been conducted, so further investigations related to this are warranted. Further detailed clinical trial experiments should be conducted for the scientific validation.

Conflict of interest statement :

Authors declare that they have no conflict of interest.

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